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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/800,984	MULYE, NIRMAL	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 - 38, 40 - 73* is/are pending in the application.

4a) Of the above claim(s) *1 - 37, 49 - 53, 57, 58, 61 and 62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38, 40 - 48, 54 - 56, 59, 60, 63 - 73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed April 28, 2009, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Response to Arguments

1. Applicant's arguments with respect to the claims rejected under 35 USC 103(a) have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112 – 1st Paragraph

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 72 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. This claim recites

"soluble alginate, methyl cellulose" while the specification recites the compound "soluble alginate methyl cellulose" (¶ [0040] on p 13 of the instant specification).

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 38, 43, 44, 46, 47, 54 – 56, 59, 60, 63 – 66 and 71 – 73 are rejected under 35 U.S.C. 102(b) as being anticipated by Shah et al. (US 6,126,969).

Shah et al. discloses the mixture of a variety of ingredients that are compressed into tablets (col 8, ln 10 – 43) with formulations as set forth in Tables 1 and 2 (bridging cols 8 and 9). The tablets can be coated with a coating such as opadry but the formulations set forth in the tables relate to the ingredients present in the tablet core (col 8, ln 41 – 43). In the formulation set forth in Table 1, the tablet contains a pharmaceutically effective amount of acetaminophen, 0.883% hydroxypropylmethylcellulose (HPMC), 0.449% of the lubricant magnesium stearate, less than 3.305% maltodextrin and 6.856% microcrystalline cellulose (MCC). The ratio of cellulose (HPMC and MCC) to maltodextrin is 1:2.3, assuming 3.305% maltodextrin is present. In this composition, cellulose and maltodextrin are about 11% by weight of the

core formulation. The amounts set forth for these same ingredients are slightly different in the formulation of Table 2, with a ratio of total cellulose compounds to maltodextrin of 2.6:1 and about 8% of the core by weight being comprised of the cellulose and maltodextrin components. The ranges recited for the total amount of cellulose and maltodextrin present in the composition are expanded beyond the numerical values recited because of the use of the word “about” and therefore the amounts present in the compositions of Shah et al. anticipate the claims of the instant application

6. Claims 38, 43, 54 – 56, 59, 60 and 71 – 73 are rejected under 35 U.S.C. 102(b) as being anticipated by Seroff et al. (US 6,387,403).

Seroff et al. discloses a dosage form with an internal compartment comprising a bilayered compressed core with a drug layer and a push layer (components 16 and 17 respectively in figure 2). In Example 4B (col 22, ln 24 – 50), the drug layer comprises a pharmaceutically acceptable amount of reboxeinate methanesulfonate, maltodextrin and stearic acid, a lubricant. The push layer comprises polyethylene oxide, which reads on a hydrophilic polymer that is sustained release carrier (see claim 71 of the instant application), hydropropyl methyl cellulose 2910 (HPMC) and magnesium stearate, a lubricant. The ratio of cellulose to maltodextrin in this composition is 1:28. Based on the total weight of the composition, the composition comprises approximately 38% maltodextrin and 1.4% HPMC.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 38, 43, 44, 46, 47, 54 – 56, 59, 60, 63 – 66 and 71 – 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shah et al. (US 6,126,969).

Shah et al. discloses the mixture of a variety of ingredients that are compressed into tablets (col 8, ln 10 – 43) with formulations as set forth in Tables 1 and 2 (bridging cols 8 and 9). The tablets can be coated with a coating such as opadry but the formulations set forth in the tables relate to the ingredients present in the tablet core (col 8, ln 41 – 43). In the formulation set forth in Table 1, the tablet contains a pharmaceutically effective amount of acetaminophen, 0.883% hydroxypropylmethylcellulose (HPMC), 0.449% of the lubricant magnesium stearate, less than 3.305% maltodextrin and 6.856% microcrystalline cellulose (MCC). The ratio

of cellulose (HPMC and MCC) to maltodextrin is 1:2.3, assuming 3.305% maltodextrin is present. In this composition, cellulose and maltodextrin are about 11% by weight of the core formulation. The amounts set forth for these same ingredients are slightly different in the formulation of Table 2, with a ratio of total cellulose compounds to maltodextrin of 2.6:1 and about 8% of the core by weight being comprised of the cellulose and maltodextrin components.

Shah et al. does not explicitly disclose formulations that contain between 20% to 50% of cellulose and maltodextrin.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to alter the amount of ingredients such as HPMC present in the composition. The person of ordinary skill in the art would have been motivated to make those modifications and reasonably would have expected success because HPMC is well-known and commonly used pharmaceutical excipient that acts a binder to impart cohesive properties to powdered material (see US 6,248,363, col 39, ln 31 – 37). Therefore the amount of HPMC and any other ingredients which can act as binders present in the composition will determine the ease with which tablets can be formed and the physical properties (e.g., hardness and friability) of the tablets which are formed. The amount of a specific ingredient such as HPMC in a composition is thus a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have

been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results.

10. Claims 38, 40 – 44, 46 – 48, 54 – 56, 59, 60 and 63 - 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shah et al. as applied to claims 38, 43, 44, 46, 47, 54 – 56, 59, 60, 63 – 66 and 71 – 73 above, and further in view of Mulye et al. (US 6,416,786).

Shah et al. discloses compositions comprising drug, maltodextrin, magnesium stearate, MCC and HPMC.

Shah et al. does not disclose xanthan gum in conjunction with a cellulose ether as the sustained release material or the use of silicified MCC (SMCC).

Mulye et al. discloses a solid sustained release tablet comprising a hydrocolloid such as xanthan gum and a cellulose ether as the sustained release carrier (abstract). A variety of active ingredients can be included in the sustained release formulation (col 3, ln 65 – col 4, ln 25). The amount of hydrocolloid and cellulose ether present are preferably between about 1:0.01 to about 1:2, or more preferably 1:0.05 to about 1:0.4 (col 6, ln 37 – 41). Hydroxypropylmethylcellulose in various forms are disclosed as suitable for the cellulose ether fraction of the sustained release carrier (col 4, ln 44 – 67). A filler such as the pharmaceutically acceptable saccharide microcrystalline cellulose can also be included (col 7, ln 3 – 17). In example 1 (col 9, ln 57 – 63), niacin, xanthan gum (XG), HPMC, SMCC and talc are made into tablets. The ratio of

XG:HPMC is 1:0.5. The other non-comparative examples make use of xanthan gum and HPMC with SMCC, although the ratio of XG:HPMC varies.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to incorporate a cellulose ether and xanthan gum sustained release carrier into the formulations of Shah et al. The person of ordinary skill in the art would have been motivated to make those modifications and reasonably would have expected success because Mulye et al. discloses that this combination of polymers is useful as a sustained release carrier. The different sustained release materials and combinations of materials will provide for different release profiles of the active ingredient. Based on the desired properties, one of ordinary skill in the art would select an appropriate sustained release carrier and other excipients that provides the desired release profile of the particular active ingredient present in the dosage form.

11. Claims 38, 43, 44, 46 – 48, 54 – 56, 59, 60 and 63 – 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shah et al. as applied to claims 38, 43, 44, 46, 47, 54 – 56, 59, 60, 63 – 66 and 71 – 73 above, and further in view of Tobyn et al. (Intl J Pharm 1998).

Shah et al. discloses compositions comprising drug, maltodextrin, magnesium stearate, MCC and HPMC.

Shah et al. does not disclose the use of silicified microcrystalline cellulose (SMCC).

Tobyn et al. discloses the MCC is widely used as a filler and binder for wet granulation, direct compression tabletting and as a filler for hard gelatin capsules (p 183, col 1, ¶1) and it has been rated as the most useful filler for direct compression tabletting (p 183, col 2, ¶1). While MCC is very useful, SMCC possesses a number of advantages in terms of powder flow, tablet strength, lubricant sensitivity and wet granulation (p 184, col 2, ¶ 1).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to incorporate SMCC into the composition of Shah et al. that comprises drug, maltodextrin, magnesium stearate, MCC and HPMC. The person of ordinary skill in the art would have been motivated to make those modifications, because and reasonably would have expected success because Tobyn et al discloses that SMCC is useful in the tabletting process with improved properties over non-silicified MCC used in Shah et al.

12. Claims 38, 43 – 47, 54 – 56, 59, 60, 63 – 66 and 71 – 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shah et al. as applied to claims 38, 43, 44, 46, 47, 54 – 56, 59, 60, 63 – 66 and 71 – 73 above, and further in view of Shell et al. (US 6,340,475).

Shah et al. discloses compositions comprising drug, maltodextrin, magnesium stearate, MCC and HPMC.

Shah et al. does not disclose metformin as an active ingredient which can be included in the formulation.

Shell et al. discloses controlled release formulations that release the drugs, such as highly soluble drugs, over extended periods of time which provide a number of improvements verses non–controlled release formulations (col 1, ln 12 – 43). Among the drugs that are highly water soluble which would benefit from being released in a controlled manner is metformin hydrochloride (col 7, ln 39 – 41).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to prepare a dosage form comprising active ingredient, HPMC, MCC, maltodextrin and lubricant and to incorporate metformin as the active pharmaceutical ingredient. The person of ordinary skill in the art would have been motivated to make those modifications in order to prepare a controlled release dosage form of metformin to administer to diabetic individuals and reasonably would have expected success because Shah et al. teaches that the compositions can be used generally for the delivery of pharmaceutical agents other than the exemplified acetaminophen (col 2, ln 47 – 54).

13. Claims 38, 40 – 47, 54 – 56, 59, 60, 63 – 66 and 71 – 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seroff et al. (US 6,387,403) in view of Shell et al. (US 6,340,475).

Seroff et al. discloses a dosage form with an internal compartment comprising a bilayered compressed core with a drug layer and a push layer (components 16 and 17 respectively in figure 2). In Example 4B (col 22, ln 24 – 50), the drug layer comprises a pharmaceutically acceptable amount of reboxeinate methanesulfonate, maltodextrin

and stearic acid, a lubricant. The push layer comprises polyethylene oxide, which reads on a hydrophilic polymer that is sustained release carrier (see claim 71 of the instant application), hydroxypropyl methyl cellulose 2910 (HPMC) and magnesium stearate, a lubricant. The ratio of cellulose to maltodextrin in this composition is 1:28. Based on the total weight of the composition, the composition comprises approximately 38% maltodextrin and 1.4% HPMC.

Seroff et al. does not disclose the use of a combination of cellulose ether and xanthan gum, microcrystalline cellulose or metformin.

Shell et al. discloses compositions wherein drug release is accomplished by the imbibition of water by hydrophilic polymers (abstract). The water-swellable polymers can be made from a variety of materials, including a variety of celluloses, including microcrystalline cellulose (col 7, ln 62), hydroxymethyl-cellulose, hydroxyethyl cellulose, HPMC and carboxymethyl cellulose (col 8, ln 15 – 17). The polymers can be used individually or in combination as certain combinations will often provide a more controlled release of drug than the components when used individually, such as cellulose-based polymers with gums (col 9, ln 42 – 48). For example, in example 6 the samples represented by open triangles are a combination of hydroxyethylcellulose (a cellulose ether) and xanthan gum (1:1 ratio; col 15, ln 16 – 21). Both hydroxy ethylcellulose and HPMC are particularly preferred as the cellulose polymer (col 8, ln 23 – 25). Among the drugs that are highly water soluble which would benefit from being released in a controlled manner is metformin hydrochloride (col 7, ln 39 – 41).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to incorporate the water-imbibing polymers and combinations of polymers as the push layer of the pharmaceutical dosage forms of Seroff et al. The person of ordinary skill in the art would have been motivated to make those modifications and reasonably would have expected success as the push layer of Seroff et al. and water-soluble polymers that imbibe water in the dosage form of Shell et al. are the same and actuate drug release in the same manner. Shell et al. discloses that a combination of polymers can provide better controlled release than the individual components. Thus one of ordinary skill in the art would select water-soluble polymers and/or combinations of water soluble polymers, such either hydroxyethylcellullose or HPMC with xanthan gum, that provide an appropriate rate of swelling and thus control release of the active ingredient. The polymers used and the amount of these ingredients are results effective parameters that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results.

Shell et al. also teaches metformin as one active ingredient that can be released in a controlled fashion to provide a variety of benefits. Thus one of ordinary skill in the art would prepare a controlled dosage form with metformin as the active ingredient.

14. Claims 38, 40 – 48, 54 – 56, 59, 60 and 63 – 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seroff et al. and Shell et al. as applied to claims 38, 40 – 47, 54 – 56, 59, 60, 63 – 66 and 71 – 73 above, and further in view of Tobyn et al. (Intl J Pharm 1998).

Seroff et al. and Shell et al. disclose compositions comprising water-swellable polymers, such as HEC, HPMC and poly(alkylene oxides) alone or in combination with gums such as xanthan gum. The selection of the polymers and the amounts of those polymers will control the rate of water-swelling and thus the release rate of the drug. The compositions provide for the controlled release of active ingredients like metformin over time.

Shah et al. does not disclose the use of silicified microcrystalline cellulose (SMCC).

Tobyn et al. discloses the MCC is widely used as a filler and binder for wet granulation, direct compression tabletting and a filler for hard gelatin capsules (p 183, col 1, ¶1) and it has been rated as the most useful filler for direct compression tabletting (p 183, col 2, ¶1). While MCC is very useful, SMCC possesses a number of advantages in terms of powder flow, tablet strength, lubricant sensitivity and wet granulation (p 184, col 2, ¶ 1).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to incorporate SMCC in place of MCC into the formulations of Seroff et al. and Shah et al. The person of ordinary skill in the art would have been motivated to make those modifications and reasonably would have expected success

because Tobyn et al. teaches the improved behavior of SMCC when formulations are prepared.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. This application contains claims 39, 49 – 53, 57, 58, 61 and 62 drawn to an invention nonelected with traverse in the reply filed on December 13, 2007. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

NMW